

L Number	Hits	Search Text	DB	Time stamp
6	0	AAV same (Srivastava.au.)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 15:47
7	0	Srivastava.au.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 15:47
8	3533	aav	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 15:47
9	5	"9809524"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 15:47
-	0	09/720066	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:51
-	0	"199967393"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/09 13:12
-	1	"99/67393"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/09 13:13
-	0	PCT/EP99/04288	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/09 13:13
-	721	AAV and infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:01
-	155	AAV same infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:01
-	123	AAV same (structural adj protein or VP1 or VP2 or VP3) and infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:02
-	8	AAV same (structural adj protein or VP1 or VP2 or VP3) same infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:04
-	64	AAV same (structural adj protein or VP1 or VP2 or VP3) and (increased or increase or efficient or improved) same infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:04

-	8	AAV same (structural adj protein or VP1 or VP2 or VP3) and (increased or increase or efficient or improved) adj15 infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 15:46
-	113	AAV same (structural adj protein or VP1 or VP2 or VP3) and (increased or increase or efficient or improved) adj15 (infection or infectivity)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:31
-	0	AAV same (structural adj protein or VP1 or VP2 or VP3) same (increased or increase or efficient or improved) adj15 infectivity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:33
-	3	AAV same (increased or increase or efficient or improved) adj15 infectivity and (mutation or insertion or deletion) same (structural adj protein or VP1 or VP2 or VP3)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/10 14:34
-	95	monoclonal adj3 antibody adj3 CD34	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:51
-	0	monoclonal adj3 antibody adj3 CD34 same sFv	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:52
-	2	monoclonal adj3 antibody adj3 CD34 same sequence	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:52
-	0	sFv adj3 CD34	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:52
-	0	sFv same CD34	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:52
-	4	single adj chain adj antibody adj3 CD34	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:55
-	0	YKQIS	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:56
-	0	SQSGA	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:56
-	0	YLTLN	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:56
-	0	NGSQA	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/09/11 13:56

=> file medline caplus  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FILE 'MEDLINE' ENTERED AT 14:45:10 ON 10 SEP 2003

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=> s AAV (S) (structural (A) protein or VP1 or VP2 or VP3) and (increased or increase or efficient or improved) (5A) (infectivity or infection)

L1 1 AAV (S) (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (INCREASED OR INCREASE OR EFFICIENT OR IMPROVED) (5A) (INFECTIVITY OR INFECTION)

=> d ibib abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:576422 CAPLUS

DOCUMENT NUMBER: 129:288869

TITLE: Development of novel cell surface CD34-targeted recombinant adenoassociated virus vectors for gene therapy

AUTHOR(S): Yang, Qicheng; Mamounas, Michael; Yu, Gang; Kennedy, Scott; Leaker, Brian; Merson, James; Wong-Staal, Flossie; Yu, Mang; Barber, Jack R.

CORPORATE SOURCE: Immusol, Inc., San Diego, CA, 92121, USA

SOURCE: Human Gene Therapy (1998), 9(13), 1929-1937  
CODEN: HGTHE3; ISSN: 1043-0342

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recombinant adeno-assocd. virus (rAAV) type 2 vectors have been used to transduce a wide variety of cell types, including hematopoietic progenitor cells. For in vivo gene transfer, it is desirable to have an rAAV vector that specifically transduces selected target cells. As a first step toward generating an rAAV vector capable of targeting delivery in vivo, the authors engineered a chimeric protein combining the AAV capsid protein and the variable region of a single-chain antibody against human CD34 mols., a cell surface marker for hematopoietic stem/progenitor cells. Inclusion of the chimeric CD34 single-chain antibody-AAV capsid proteins within an rAAV virion significantly **increased** the preferential **infectivity** of rAAV for the CD34+ human myoleukemia cell line KG-1, which is normally refractory to rAAV transduction. Antibodies against the single-chain antibody and the CD34 protein blocked this transduction. This chimeric vector represents a significant improvement in the host range of rAAV and the first step toward specific gene delivery by rAAV vectors to cells of choice, in this case, hematopoietic progenitor cells, for the treatment of human disease. The authors constructed rAAV type 2 vectors encoding modified capsid proteins that allow for cell-type specific targeting to cells that express the CD34 protein. A fusion protein was constructed, consisting of the N terminus of the **AAV**

virion protein, VP2, and a single-chain antibody directed against CD34. Vector particles packaged in the presence of the VP2-antibody fusion protein are bound specifically to CD34-expressing KG-1 cells. Moreover, while KG-1 cells were resistant to transduction by unmodified rAAV vectors, the modified vector particles were able to transduce these cells. Antibodies against either the CD34 mol. or the single-chain antibody blocked the modified rAAV virion transduction of KG-1 cells. Thus, the tropism of the rAAV particle can be altered by addn. of chimeric capsid fusion proteins during viral particle formation.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST	0.12	25.76
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=> s AAV and structural (A) protein or VP1 or VP2 or VP3) same (increased or increase or efficient or improved) (5A) (infectivity or infection)  
 UNMATCHED RIGHT PARENTHESIS 'VP3) SAME'  
 The number of right parentheses in a query must be equal to the number of left parentheses.

=> s AAV and (structural (A) protein or VP1 or VP2 or VP3) same (increased or increase or efficient or improved) (5A) (infectivity or infection)  
 MISSING OPERATOR VP3) SAME  
 The search profile that was entered contains terms or

nested terms that are not separated by a logical operator.

=> s AAV and structural (A) protein or VP1 or VP2 or VP3) (S) (increased or increase or efficient or improved) (5A) (infectivity or infection)

UNMATCHED RIGHT PARENTHESIS 'VP3) '

The number of right parentheses in a query must be equal to the number of left parentheses.

=> s AAV and (structural (A) protein or VP1 or VP2 or VP3) (s) (increased or increase or efficient or improved) (5A) (infectivity or infection)

L2           0 AAV AND (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) (S) (INCREASED OR INCREASE OR EFFICIENT OR IMPROVED) (5A) (INFECTIVITY OR INFECTION)

=> s AAV and (structural (A) protein or VP1 or VP2 or VP3) and (increased or increase or efficient or improved) (5A) (infectivity or infection)

L3           1 AAV AND (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (INCREASED OR INCREASE OR EFFICIENT OR IMPROVED) (5A) (INFECTIVITY OR INFECTION)

=> d ibib abs

L3   ANSWER 1 OF 1   CAPLUS   COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:       1998:576422   CAPLUS

DOCUMENT NUMBER:       129:288869

TITLE:                Development of novel cell surface CD34-targeted recombinant adenoassociated virus vectors for gene therapy

AUTHOR(S):            Yang, Qicheng; Mamounas, Michael; Yu, Gang; Kennedy, Scott; Leaker, Brian; Merson, James; Wong-Staal, Flossie; Yu, Mang; Barber, Jack R.

CORPORATE SOURCE:     Immusol, Inc., San Diego, CA, 92121, USA

SOURCE:              Human Gene Therapy (1998), 9(13), 1929-1937

CODEN: HGTHE3; ISSN: 1043-0342

PUBLISHER:            Mary Ann Liebert, Inc.

DOCUMENT TYPE:        Journal

LANGUAGE:             English

AB   Recombinant adeno-assocd. virus (rAAV) type 2 vectors have been used to transduce a wide variety of cell types, including hematopoietic progenitor cells. For in vivo gene transfer, it is desirable to have an rAAV vector that specifically transduces selected target cells. As a first step toward generating an rAAV vector capable of targeting delivery in vivo, the authors engineered a chimeric protein combining the AAV capsid protein and the variable region of a single-chain antibody against human CD34 mols., a cell surface marker for hematopoietic stem/progenitor cells. Inclusion of the chimeric CD34 single-chain antibody-AAV capsid proteins within an rAAV virion significantly **increased** the preferential **infectivity** of rAAV for the CD34+ human myoleukemia cell line KG-1, which is normally refractory to rAAV transduction. Antibodies against the single-chain antibody and the CD34 protein blocked this transduction. This chimeric vector represents a significant improvement in the host range of rAAV and the first step toward specific gene delivery by rAAV vectors to cells of choice, in this case, hematopoietic progenitor cells, for the treatment of human disease. The authors constructed rAAV type 2 vectors encoding modified capsid proteins that allow for cell-type specific targeting to cells that express

the CD34 protein. A fusion protein was constructed, consisting of the N terminus of the AAV virion protein, VP2, and a single-chain antibody directed against CD34. Vector particles packaged in the presence of the VP2-antibody fusion protein are bound specifically to CD34-expressing KG-1 cells. Moreover, while KG-1 cells were resistant to transduction by unmodified rAAV vectors, the modified vector particles were able to transduce these cells. Antibodies against either the CD34 mol. or the single-chain antibody blocked the modified rAAV virion transduction of KG-1 cells. Thus, the tropism of the rAAV particle can be altered by addn. of chimeric capsid fusion proteins during viral particle formation.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s AAV and (structural (A) protein or VP1 or VP2 or VP3) and (infectivity or infection)

L4 37 AAV AND (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (INFECTIVITY OR INFECTION)

=> s AAV (S) (structural (A) protein or VP1 or VP2 or VP3) and (infectivity or infection)

L5 22 AAV (S) (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (INFECTIVITY OR INFECTION)

=> s AAV (S) (structural (A) protein or VP1 or VP2 or VP3) (S) (infectivity or infection)

L6 4 AAV (S) (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) (S) (INFECTIVITY OR INFECTION)

=> dup rem l6

PROCESSING COMPLETED FOR L6

L7 3 DUP REM L6 (1 DUPLICATE REMOVED)

=> d ibib abs 1-3

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:678569 CAPLUS

DOCUMENT NUMBER: 133:333831

TITLE: Monoclonal antibodies against the adeno-associated virus type 2 (AAV-2) capsid: epitope mapping and identification of capsid domains involved in AAV-2-cell interaction and neutralization of AAV-2 infection

AUTHOR(S): Wobus, Christiane E.; Hugle-Dorr, Barbara; Girod, Anne; Petersen, Gabriele; Hallek, Michael; Kleinschmidt, Jurgen A.

CORPORATE SOURCE: Forschungsschwerpunkt Angewandte Tumorstudiologie, Deutsches Krebsforschungszentrum, Heidelberg, D-69120, Germany

SOURCE: Journal of Virology (2000), 74(19), 9281-9293  
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The previously characterized monoclonal antibodies (MAbs) A1, A69, B1, and

A20 are directed against assembled or nonassembled adeno-assocd. virus type 2 (AAV-2) capsid proteins. Here we describe the linear epitopes of A1, A69, and B1 which reside in VP1, VP2, and VP3, resp., using gene fragment phage display library, peptide scan, and peptide competition expts. In addn., MAbs A20, C24-B, C37-B, and D3 directed against conformational epitopes on AAV-2 capsids were characterized. Epitope sequences on the capsid surface were identified by enzyme-linked immunoabsorbent assay using AAV-2 mutants and AAV serotypes, peptide scan, and peptide competition expts. A20 neutralizes infection following receptor attachment by binding an epitope formed during AAV-2 capsid assembly. The newly isolated antibodies C24-B and C37-B inhibit AAV-2 binding to cells, probably by recognizing a loop region involved in binding of AAV-2 to the cellular receptor. In contrast, binding of D3 to a loop near the predicted threefold spike does not neutralize AAV-2 infection. The identified antigenic regions on the AAV-2 capsid surface are discussed with respect to their possible roles in different steps of the viral life cycle.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1  
 ACCESSION NUMBER: 93059635 MEDLINE  
 DOCUMENT NUMBER: 93059635 PubMed ID: 1331503  
 TITLE: Assembly of viruslike particles by recombinant structural proteins of adeno-associated virus type 2 in insect cells.  
 AUTHOR: Ruffing M; Zentgraf H; Kleinschmidt J A  
 CORPORATE SOURCE: Deutsches Krebsforschungszentrum, Forschungsschwerpunkt Angewandte Tumorstudiologie, Heidelberg, Germany.  
 SOURCE: JOURNAL OF VIROLOGY, (1992 Dec) 66 (12) 6922-30.  
 Journal code: 0113724. ISSN: 0022-538X.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199212  
 ENTRY DATE: Entered STN: 19930122  
 Last Updated on STN: 19970203  
 Entered Medline: 19921215

AB The three capsid proteins VP1, VP2, and VP3 of the adeno-associated virus type 2 (AAV-2) are encoded by overlapping sequences of the same open reading frame. Separate expression of these proteins by recombinant baculoviruses in insect cells was achieved by mutation of the internal translation initiation codons. Coexpression of VP1 and VP2, VP2 and VP3, and all three capsid proteins and the expression of VP2 alone in Sf9 cells resulted in the production of viruslike particles resembling empty capsids generated during infection of HeLa cells with AAV-2 and adenovirus. These results suggest a requirement for VP2 in the formation of empty capsids. Individual expression of the AAV capsid proteins in HeLa cells showed that VP1 and VP2 accumulate in the cell nucleus and VP3 is distributed between nucleus and cytoplasm. Coexpression of VP3 with the other structural proteins also led to nuclear localization of VP3, indicating that the formation of a complex with VP1 or VP2 is required for accumulation of VP3 in the nucleus.

L7 ANSWER 3 OF 3 MEDLINE on STN

ACCESSION NUMBER: 77229536 MEDLINE  
 DOCUMENT NUMBER: 77229536 PubMed ID: 881618  
 TITLE: Complementation of adeno-associated satellite virus (AAV) by temperature-sensitive mutants of adenovirus type 31.  
 AUTHOR: Mayor H D; Carrier S; Jordan L  
 SOURCE: JOURNAL OF GENERAL VIROLOGY, (1977 Jun) 35 (3) 545-53.  
 Journal code: 0077340. ISSN: 0022-1317.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 197709  
 ENTRY DATE: Entered STN: 19900314  
 Last Updated on STN: 19900314  
 Entered Medline: 19770917

AB Temperature-sensitive (ts) mutants of human adenovirus type 31 were able to complement adeno-associated satellite virus (AAV) antigen production in both HEK and KB cells at both permissive and non-permissive temperatures. However, mutant ts 94, an adenovirus 31 mutant which produces apparently normal amounts of **structural protein** and DNA but is defective in maturation, was significantly inhibited in its ability to potentiate **AAV infectivity** at the non-permissive temperature. Normal AAV DNA and adenovirus DNA were isolated from co-infections with AAV and mutant ts 94 at the non-permissive temperature. We suggest that an adenovirus-coded maturation function common to both adenovirus and AAV maturation is defective in the ts 94 system.

=> s (mutant or mutated or mutate) (10A) (structural or VP1 or VP2 or VP3). (S) AAV  
 L8 5 (MUTANT OR MUTATED OR MUTATE) (10A) (STRUCTURAL OR VP1 OR VP2 OR VP3) (S) AAV

=> dup rem l8  
 PROCESSING COMPLETED FOR L8  
 L9 3 DUP REM L8 (2 DUPLICATES REMOVED)

=> d ibib abs 1-3

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 2002:869930 CAPLUS  
 DOCUMENT NUMBER: 138:150022  
 TITLE: Addition of six-His-tagged peptide to the C terminus of adeno-associated virus VP3 does not affect viral tropism or production  
 AUTHOR(S): Zhang, Huang-Ge; Xie, Jinfu; Dmitriev, Igor; Kashentseva, Elena; Curiel, David T.; Hsu, Hui-Chen; Mountz, John D.  
 CORPORATE SOURCE: Division of Clinical Immunology and Rheumatology, Department of Medicine, The University of Alabama at Birmingham, Birmingham, AL, 35294, USA  
 SOURCE: Journal of Virology (2002), 76(23), 12023-12031  
 CODEN: JOVIAM; ISSN: 0022-538X  
 PUBLISHER: American Society for Microbiology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Prod. of large quantities of recombinant adeno-assocd. virus (AAV) is



difficult and not cost-effective. To overcome this problem, we have explored the feasibility of creating a recombinant AAV encoding a 6.times.His tag on the VP3 capsid protein. We generated a plasmid vector contg. a six-His (6.times.His)-tagged AAV VP3. A second plasmid vector was generated that contained the full-length AAV capsid capable of producing VP1 and VP2, but not VP3 due to a mutation at position 2809 that encodes the start codon for VP3. These plasmids, necessary for prodn. of AAV, were transfected into 293 cells to generate a

6.times.His-tagged **VP3 mutant** recombinant **AAV**

. The 6.times.His-tagged VP3 did not affect the formation of AAV virus, and the phys. properties of the 6.times.His-modified AAV were equiv. to those of wild-type particles. The 6.times.His-tagged AAV did not affect the prodn. titer of recombinant AAV and could be used to purify the recombinant AAV using an Ni-nitrilotriacetic acid column. Addn. of the 6.times.His tag did not alter the viral tropism compared to wild-type AAV. These observations demonstrate the feasibility of producing high-titer AAV contg. a 6.times.His-tagged AAV VP3 capsid protein and to utilize the 6.times.His-tagged VP3 capsid to achieve high-affinity purifn. of this recombinant AAV.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2000070317 MEDLINE  
DOCUMENT NUMBER: 20070317 PubMed ID: 10600599  
TITLE: Insertional mutagenesis of AAV2 capsid and the production of recombinant virus.  
AUTHOR: Rabinowitz J E; Xiao W; Samulski R J  
CORPORATE SOURCE: The Gene Therapy Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.  
CONTRACT NUMBER: DK53423-01 (NIDDK)  
HL51818-06 (NHLBI)  
SOURCE: VIROLOGY, (1999 Dec 20) 265 (2) 274-85.  
Journal code: 0110674. ISSN: 0042-6822.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200002  
ENTRY DATE: Entered STN: 20000209  
Last Updated on STN: 20021218  
Entered Medline: 20000202

AB The structural genes of adeno-associated virus serotype 2 (AAV2) have been altered by linker insertional mutagenesis in order to define critical components of virion assembly and infectivity. An in-frame restriction site linker was inserted across the capsid coding domain of a recombinant plasmid. After complementation in vivo, recombinant AAV2 viruses were generated and assayed for capsid production, packaging, transduction, heparin agarose binding, and morphology. Three classes of capsid mutants were identified. Class I mutants expressed structural proteins but were defective in virion assembly. Class II mutants generated intact virions that protected the viral genome from DNase, but failed to infect target cells. The majority of these mutants bound the heparin affinity matrix, suggesting that attachment to the AAV primary receptor was not rate limiting. One class II **mutant**, H2634, assembled virions and bound heparin using only **Vp3**, indicating that this subunit is

responsible for mediating AAV receptor attachment. Finally, class III mutants assembled virions, encapsidated DNA, and infected target cells. Infectivity of these mutants ranged from 5 to 100% of that of the wild-type, demonstrating for the first time the ability to alter capsid proteins without interfering with infectivity. These AAV virions with altered capsid subunits will provide critical templates for manipulating AAV vectors for cell-specific gene delivery in vivo. In summary, the AAV capsid variants described here will facilitate further study of virus assembly, entry, and infection, as well as advance the development of this versatile vector system.

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L9 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 77229536 MEDLINE

DOCUMENT NUMBER: 77229536 PubMed ID: 881618

TITLE: Complementation of adeno-associated satellite virus (AAV) by temperature-sensitive mutants of adenovirus type 31.

AUTHOR: Mayor H D; Carrier S; Jordan L

SOURCE: JOURNAL OF GENERAL VIROLOGY, (1977 Jun) 35 (3) 545-53.  
Journal code: 0077340. ISSN: 0022-1317.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 197709

ENTRY DATE: Entered STN: 19900314  
Last Updated on STN: 19900314  
Entered Medline: 19770917

AB Temperature-sensitive (ts) mutants of human adenovirus type 31 were able to complement adeno-associated satellite virus (AAV) antigen production in both HEK and KB cells at both permissive and non-permissive temperatures. However, mutant ts 94, an adenovirus 31 mutant which produces apparently normal amounts of structural protein and DNA but is defective in maturation, was significantly inhibited in its ability to potentiate AAV infectivity at the non-permissive temperature. Normal AAV DNA and adenovirus DNA were isolated from co-infections with AAV and mutant ts 94 at the non-permissive temperature. We suggest that an adenovirus-coded maturation function common to both adenovirus and AAV maturation is defective in the ts 94 system.

=> d his

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FILE 'MEDLINE, CAPLUS' ENTERED AT 14:45:10 ON 10 SEP 2003

L1 1 S AAV (S) (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (IN

FILE 'STNGUIDE' ENTERED AT 14:48:34 ON 10 SEP 2003

FILE 'MEDLINE, CAPLUS' ENTERED AT 14:50:01 ON 10 SEP 2003

L2 0 S AAV AND (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) (S) (IN

L3 1 S AAV AND (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (IN

L4 37 S AAV AND (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (IN

L5 22 S AAV (S) (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) AND (IN

L6 4 S AAV (S) (STRUCTURAL (A) PROTEIN OR VP1 OR VP2 OR VP3) (S) (IN

L7 3 DUP REM L6 (1 DUPLICATE REMOVED)  
L8 5 S (MUTANT OR MUTATED OR MUTATE) (10A) (STRUCTURAL OR VP1 OR VP2)  
L9 3 DUP REM L8 (2 DUPLICATES REMOVED)

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NEWS	4	Feb 24	TEMA now available on STN
NEWS	5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	6	Feb 26	PCTFULL now contains images
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NEWS 30 AUG 13 Field Availability (/FA) field enhanced in BEILSTEIN  
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 September 2003  
 NEWS 32 AUG 15 PCTGEN: one FREE connect hour, per account, in  
 September 2003  
 NEWS 33 AUG 15 RDISCLOSURE: one FREE connect hour, per account, in  
 September 2003  
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 September 2003  
 NEWS 35 AUG 18 Data available for download as a PDF in RDISCLOSURE  
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 NEWS 37 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right  
 Truncation  
 NEWS 38 AUG 18 Simultaneous left and right truncation added to ANABSTR

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT  
 MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
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FILE 'HOME' ENTERED AT 13:58:24 ON 11 SEP 2003

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=> file medline caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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L1 13 SINGLE (A) CHAIN (A) ANTIBODY (S) CD34

=> dup rem l1  
PROCESSING COMPLETED FOR L1  
L2 9 DUP REM L1 (4 DUPLICATES REMOVED)

=> d ibib abs 1-9

L2 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2001284813 MEDLINE  
DOCUMENT NUMBER: 21142084 PubMed ID: 11209088  
TITLE: Anti-VEGFR-2 scFvs for cell isolation. **Single-chain antibodies** recognizing the human vascular endothelial growth factor receptor-2 (VEGFR-2/flk-1) on the surface of primary endothelial cells and preselected **CD34+** cells from cord blood.  
AUTHOR: Boldicke T; Tesar M; Griesel C; Rohde M; Grone H J; Waltenberger J; Kollet O; Lapidot T; Yayon A; Weich H  
CORPORATE SOURCE: German Research Centre for Biotechnology, Department of Applied Genetics, Braunschweig, Germany.. tbo@gbf.de  
SOURCE: STEM CELLS, (2001) 19 (1) 24-36.  
Journal code: 9304532. ISSN: 1066-5099.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 20010529  
Last Updated on STN: 20010529  
Entered Medline: 20010524

AB Five specific single-chain antibodies recognizing the human vascular endothelial growth factor receptor-2 (VEGFR-2/KDR) were selected from a V-gene phage display library constructed from mice immunized with the extracellular domain of VEGFR-2 (Ig-like domain 1-7). All five scFv antibodies (A2, A7, B11, G3, and H1) bound to the purified native antigen in enzyme-linked immunosorbent assay and Dot Blot, and showed no crossreactivity to the human VEGF-receptor 1 (VEGFR-1). The selected antibodies recognize a conformation-dependent epitope of the native receptor and do not recognize denatured antigen in Western blots, as well as linear overlapping peptides comprising the sequence of the human VEGFR-2. The five scFv antibodies bind to the surface of endothelial cells overexpressing human VEGFR-2 c-DNA (PAE/VEGFR-2 cells) as detected by surface immunofluorescence using confocal microscopy. In addition scFv A7 specifically detected VEGFR-2 expressing endothelial cells in the glomerulus of frozen human kidney tissue sections. Therefore, A7 has potential clinical application as a marker for angiogenesis in cryosections of different human tissues. Additionally, two recombinant scFvs (A2 and A7) very efficiently recognize VEGFR-2 on PAE/VEGFR-2 cells and freshly prepared human umbilical vein endothelial cells by fluorescence-activated cell sorter (FACS) analysis. The scFv fragment A7, which was the most sensitive antibody in FACS analysis, recognizes human CD34+VEGFR-2+ hematopoietic immature cells within the population of enriched CD34+ cells isolated from human cord blood. The dissociation constant of A7 was determined to be  $K(d) = 3.8 \times 10^{-9}$  M by BIAcore analysis. In conclusion, scFv fragment A7 seems to be an important tool

for FACS analysis and cell sorting of vascular endothelial cells, progenitor cells and hematopoietic stem cells, which are positive for VEGFR-2 gene expression.

L2 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:692016 CAPLUS

DOCUMENT NUMBER: 132:22064

TITLE: Inhibition of human immunodeficiency virus replication and growth advantage of CD4+ T cells and monocytes derived from CD34+ cells transduced with an intracellular antibody directed against human immunodeficiency virus type 1 tat

AUTHOR(S): Poznansky, Mark C.; La Vecchio, Joyce; Silva-Arietta, Sandra; Porter-Brooks, Julie; Brody, Kate; Olszak, Ivona T.; Adams, Gregor B.; Ramstedt, Urban; Marasco, Wayne A.; Scadden, David T.

CORPORATE SOURCE: Partners AIDS Research Center and MGH Cancer Center, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02129, USA

SOURCE: Human Gene Therapy (1999), 10(15), 2505-2514  
CODEN: HGTHE3; ISSN: 1043-0342

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Current clin. gene therapy protocols for the treatment of human immunodeficiency virus type 1 (HIV-1) infection involve the ex vivo transduction and expansion of CD4+ T cells derived from HIV-pos. patients at a late stage in their disease (CD4+ cell count <400 cells/mm<sup>3</sup>). We examd. the efficiency of transduction and transgene expression in adult bone marrow (BM)- and umbilical cord blood (UCB)-derived CD34+ cells induced to differentiate into T cells and monocytes in vitro with an MuLV-based vector encoding the neomycin resistance gene and an intracellular antibody directed against the Tat protein of HIV-1 (sFvtat1-C.kappa.). The expression of the marker gene and the effects of antiviral construct on subsequent challenge with monocyto-tropic and T cell-tropic HIV-1 isolates were monitored in vitro in purified T cells and monocytes generated in culture from the transduced CD34+ cells. Transduction efficiencies of CD34+ cells ranged between 22 and 27%. Differentiation of CD34+ cells into T cells or monocytes was not significantly altered by the transduction process. HIV-1 replication in monocytes and CD4+ T cells derived from CD34+ cells transduced with the intracellular antibody gene was significantly reduced in comparison with the degree of HIV replication seen in monocytes and CD4+ T cells derived from CD34+ cells transduced with the neomycin resistance gene alone. Further, T cells and monocytes derived from CD34+ cells transduced with the intracellular antibody gene were demonstrated to express the sFvtat1-C.kappa. transgene by RT-PCR and had a selective growth advantage in cultures that had been challenged with HIV-1. These data demonstrate that sFvtat1-C.kappa. inhibits HIV-1 replication in T cells and monocytes developing from CD34+ cells and supports the continuing development of a stem cell gene therapy for the treatment of HIV-1 infection.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 9 MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 1999191986 MEDLINE

DOCUMENT NUMBER: 99191986 PubMed ID: 10094198  
TITLE: Targeting retroviral vectors to CD34-expressing cells:  
binding to CD34 does not catalyze virus-cell fusion.  
AUTHOR: Benedict C A; Tun R Y; Rubinstein D B; Guillaume T; Cannon  
P M; Anderson W F  
CORPORATE SOURCE: Gene Therapy Laboratories, Norris Cancer Center, University  
of Southern California School of Medicine, Los Angeles  
90033, USA.  
CONTRACT NUMBER: CA59318-04 (NCI)  
SOURCE: HUMAN GENE THERAPY, (1999 Mar 1) 10 (4) 545-57.  
Journal code: 9008950. ISSN: 1043-0342.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 199904  
ENTRY DATE: Entered STN: 19990517  
Last Updated on STN: 19990517  
Entered Medline: 19990430

AB We have attempted to engineer murine leukemia virus (MuLV)-based retroviral vectors to specifically transduce cells expressing human CD34, an antigen present on the surface of undifferentiated hematopoietic stem cells. A number of chimeric ecotropic MuLV envelope (Env) proteins were constructed that contained anti-CD34 **single-chain antibody** variable fragments (scFvs). The scFv-Env proteins were generated either by replacing the receptor-binding domain of Env with the scFv or by inserting the scFv into the N terminus of the Env protein. Only chimeric Env proteins with scFv insertions between amino acids 6 and 7 were incorporated into viral particles, and coexpression of native MuLV Env did not rescue incorporation-defective proteins. In addition, the efficiency of incorporation varied with the specific anti-CD34 scFv that was used. Retroviral vectors containing the scFv-Env proteins bound to CD34+ cells and transduced NIH 3T3 cells expressing human CD34 (3T3-CD34 cells) at approximately twice the efficiency of the parental NIH 3T3 cells. However, the introduction of the mutation D84K, which prevents binding to the ecotropic MuLV receptor mcat-1, prevented transduction of both NIH 3T3 and 3T3-CD34 cells. Complementation cell-cell fusion assays [Zhao et al. (1997). J. Virol. 71, 6967-6972] in 3T3-CD34 cells revealed that although the scFv-Env proteins could contribute postbinding entry functions when bound to mcat-1, they were unable to do so when bound to CD34. Taken together, these data suggest that although the interaction with CD34 effectively increased the concentration of virus on 3T3-CD34 cells, entry could occur only through an interaction with mcat-1; CD34 alone was not capable of triggering the appropriate postbinding changes that lead to viral entry.

L2 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:262557 CAPLUS  
DOCUMENT NUMBER: 131:98315  
TITLE: Construction and sequence analysis of anti-  
**CD34 single-chain  
antibody**  
AUTHOR(S): Hu, Baocheng; Pomerantz, Roger J.; Duan, Lingxun  
CORPORATE SOURCE: Institute of Biotechnology, Academy of Military  
Medical Sciences, Beijing, 100071, Peop. Rep. China  
SOURCE: Junshi Yixue Kexueyuan Yuankan (1999), 23(1), 1-4

CODEN: JYKYEL; ISSN: 1000-5501  
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB A hybridoma which can secrete anti-CD34 monoclonal antibody was used in the construction of **single-chain antibody** (sFv) gene to clone anti-CD34 **single-chain antibody** gene. The cells were used for prepn. of total cellular RNA and the cDNAs of the variable heavy chain (VH) and light chain (VL) regions were synthesized by RT-PCR. The framework regions (FR) and complementary detg. regions (CDR) of the antibody were detd. by using the Kabat antibody sequence database and new PCR primers contg. appropriate restriction enzyme sites for further cloning were used to reamplify each of the VL and VH fragments, with deletion of the remaining secretory leader sequences. The DNAs of light and heavy chain were joined together via a flexible linker to obtained anti-CD34 sFv gene. The sequence anal. demonstrated that the VL and VH belonged to kappa light chain subgroup V and heavy chain subgroup I (B) of mouse variable region resp. The complete sFv construct, including linker sequence, was 813 bp and the mol. wt. of the encoded protein is approx. 30 kDa.

L2 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:388169 CAPLUS  
DOCUMENT NUMBER: 129:94463  
TITLE: Cloning of cDNA for VH and VL of mouse monoclonal antibody to human antigen CD34 and preparation of humanized antibodies for clinical use  
INVENTOR(S): Miyamura, Koichi; Ono, Mitsuharu  
PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan; Asahi Medical Co.  
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10155489	A2	19980616	JP 1996-331647	19961127
PRIORITY APPLN. INFO.:			JP 1996-331647	19961127

AB The cDNA encoding VH and VL of the monoclonal antibody, that recognizes human antigen CD34 and is secreted by mouse hybridoma anti-My-10, is isolated and used for the prepn. of humanized antibodies or ScFV (single-chain variable fragment). Use of the recombinant antibodies as a therapeutic agent for, e.g., leukemia, is claimed.

L2 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:759396 CAPLUS  
DOCUMENT NUMBER: 130:104767  
TITLE: Cell-type-specific gene transfer into human cells with retroviral vectors that display single-chain antibodies  
AUTHOR(S): Jiang, An; Chu, Te-Hua T.; Nocken, F.; Cichutek, Klaus; Dornburg, Ralph  
CORPORATE SOURCE: Div. Infectious Diseases, Thomas Jefferson Univ.,



Philadelphia, PA, 19107, USA  
SOURCE: Journal of Virology (1998), 72(12), 10148-10156  
CODEN: JOVIAM; ISSN: 0022-538X  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The successful application of human gene therapy protocols on a broad clin. basis will depend on the availability of in vivo cell-type-specific gene delivery systems. We have developed retroviral vector particles, derived from spleen necrosis virus (SNV), that display the antigen binding site of an antibody on the viral surface. Using retroviral vectors derived from SNV that displayed single-chain antibodies (scAs) directed against a carcinoembryonic antigen-cross-reacting cell surface protein, we have shown that an efficient, cell-type-specific gene delivery can be obtained. In this study, we tested whether other scAs displayed on SNV vector particles can also lead to cell-type-specific gene delivery. We displayed the following scAs on the retroviral surface: one directed against the human cell surface antigen Her2neu, which belongs to the epidermal growth factor receptor family; one directed against the stem cell-specific antigen CD34; and one directed against the transferrin receptor, which is expressed on liver cells and various other tissues. We show that retroviral vectors displaying these scAs are competent for infection in human cells which express the antigen recognized by the scA. Infectivity was cell type specific, and titers above 105 CFU per mL of tissue culture supernatant medium were obtained. The d. of the antigen on the target cell surface does not influence virus titers in vitro. Our data indicate that the SNV vector system is well suited for the development of a large variety of cell-type-specific targeting vectors.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 9 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 1998412462 MEDLINE  
DOCUMENT NUMBER: 98412462 PubMed ID: 9741431  
TITLE: Development of novel cell surface CD34-targeted recombinant adenoassociated virus vectors for gene therapy.  
AUTHOR: Yang Q; Mamounas M; Yu G; Kennedy S; Leaker B; Merson J; Wong-Staal F; Yu M; Barber J R  
CORPORATE SOURCE: Immusol, Inc., San Diego, CA 92121, USA.  
SOURCE: HUMAN GENE THERAPY, (1998 Sep 1) 9 (13) 1929-37.  
Journal code: 9008950. ISSN: 1043-0342.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199811  
ENTRY DATE: Entered STN: 19990106  
Last Updated on STN: 19990106  
Entered Medline: 19981118

AB Recombinant adenoassociated virus (rAAV) type 2 vectors have been used to transduce a wide variety of cell types, including hematopoietic progenitor cells. For in vivo gene transfer, it is desirable to have an rAAV vector that specifically transduces selected target cells. As a first step toward generating an rAAV vector capable of targeting delivery in vivo, we have engineered a chimeric protein combining the AAV capsid protein and the variable region of a **single-chain antibody**

against human **CD34** molecules, a cell surface marker for hematopoietic stem/progenitor cells. Inclusion of the chimeric **CD34 single-chain antibody-AAV** capsid proteins within an rAAV virion significantly increased the preferential infectivity of rAAV for the **CD34+** human myoleukemia cell line KG-1, which is normally refractory to rAAV transduction. Antibodies against the **single-chain antibody** and the **CD34** protein blocked this transduction. This chimeric vector represents a significant improvement in the host range of rAAV and the first step toward specific gene delivery by rAAV vectors to cells of choice, in this case, hematopoietic progenitor cells, for the treatment of human disease.

L2 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:454058 CAPLUS  
DOCUMENT NUMBER: 127:80164  
TITLE: Single-chain antibodies with membrane-binding domains that mediate adhesion between cells and their use as co-stimulatory ligands  
INVENTOR(S): Ledbetter, Jeffrey A.; Hayden, Martha; Fell, Perry; Mittler, Robert; Winberg, Gosta  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
SOURCE: PCT Int. Appl., 69 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720048	A2	19970605	WO 1996-US19051	19961127

W: CA, JP, MX

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1995-7755P P 19951130

AB Single-chain antibodies (sFv mols.) with membrane-binding domains are described. These sFv mols. stimulate adhesion between CD4+ T-cells and antigen-presenting cells thereby increasing the immune response against disease. The antigen binding domain binds a leukocyte antigen and transmembrane domain is derived from a cell surface receptor, specifically a leukocyte antigen. Retrovirus expression vectors for sFv's using monoclonal antibodies to neural cell adhesion mol. L1 with the transmembrane domain of B7 or CD58 were constructed by std. methods. Expression of the constructs in animal cell lines led to surface presentation of the antibody.

L2 ANSWER 9 OF 9 MEDLINE on STN

DUPLICATE 4

ACCESSION NUMBER: 97203226 MEDLINE  
DOCUMENT NUMBER: 97203226 PubMed ID: 9050944  
TITLE: Determination of the binding affinity of an anti-**CD34 single-chain antibody** using a novel, flow cytometry based assay.  
AUTHOR: Benedict C A; MacKrell A J; Anderson W F  
CORPORATE SOURCE: Gene Therapy Laboratories, Norris Cancer Center, University of Southern California School of Medicine, Los Angeles 90033, USA.

SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1997 Feb 28) 201 (2)  
 223-31.  
 Journal code: 1305440. ISSN: 0022-1759.  
 PUB. COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199703  
 ENTRY DATE: Entered STN: 19970407  
 Last Updated on STN: 19970407  
 Entered Medline: 19970326

AB A single chain antibody (scFv) was constructed from a hybridoma expressing the anti-CD34 monoclonal antibody My10. The scFv was expressed in the mouse fibroblast cell line NIH 3T3, and purified from culture supernatant via an epitope tag fused to the C-terminus of the protein. The scFv equilibrium dissociation constant (KD) was determined to be  $2.4 \times 10^{-7}$  M using a fluorescence based flow cytometry assay involving recognition of the epitope tag, and bound approximately 24-fold less avidly to CD34 expressing KG-1a cells than the native antibody My10. This novel and previously unreported method for determining antibody binding affinity offers several advantages over alternative methods. It is rapid and simple, and unlike methods that directly label the antibody, it involves no covalent modifications of antibody variable domain residues that could potentially interfere with antigen binding. The KD for the anti-CD33 antibody HuG1 (Caron et al. (1992) The biological and immunological features of humanized M195 (anti-CD33) monoclonal antibodies. Cancer Res. 52, 6761-6767) was determined as well. The close agreement of this value and the previously reported value, determined by a radioligand competition method, validates the use of this assay for antibody affinity determination. We discuss various potential applications for this anti-CD34 scFv.

=> s YKQIS

L3 0 YKQIS

=> s sqsga

L4 0 SQSGA

=> s yltln

L5 0 YLTLN

=> s ngsqa

L6 0 NGSQA

=> s yylsr

L7 0 YYLSR

=> s tntps

L8 0 TNTPS

=> s eekff

L9 0 EEKFF

=> spqsgv

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L10 0 PQSGV

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NEWS 34 AUG 15 TEMA: one FREE connect hour, per account, in September 2003

NEWS 35 AUG 18 Data available for download as a PDF in RDISCLOSURE

NEWS 36 AUG 18 Simultaneous left and right truncation added to PASCAL

NEWS 37 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation

NEWS 38 AUG 18 Simultaneous left and right truncation added to ANABSTR

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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=> file medline caplus

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FULL ESTIMATED COST	0.42	0.42

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FILE 'CAPLUS' ENTERED AT 15:42:07 ON 11 SEP 2003

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L1 219 AAV AND (TARGETING OR TROPISM)

=> dup rem 11

PROCESSING COMPLETED FOR L1

L2 143 DUP REM L1 (76 DUPLICATES REMOVED)

=> s l2 and py<=1998

L3 40 L2 AND PY<=1998

=> s l3 and (VP1 or VP2 or VP3)

L4 1 L3 AND (VP1 OR VP2 OR VP3)

=> d ibib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:169418 CAPLUS

DOCUMENT NUMBER: 128:227084

TITLE: Methods and compositions for liver-specific delivery of therapeutic molecules using recombinant adeno-associated virus vectors

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PATENT ASSIGNEE(S): Chiron Corporation, USA; Indiana University

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809524	A1	19980312	WO 1997-US15453	19970902 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 933997	A1	19990811	EP 1997-940762	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500376	T2	20010116	JP 1998-512823	19970902
US 6521225	B1	20030218	US 1997-921497	19970902
US 2001051611	A1	20011213	US 2001-912680	20010724
US 2003166284	A1	20030904	US 2002-109799	20020328
PRIORITY APPLN. INFO.:			US 1996-25616P	P 19960906
			US 1996-25649P	P 19960911
			US 1997-921497	A1 19970902
			WO 1997-US15453	W 19970902

AB Provided are methods for selectively expressing therapeutic mols., such as secretory proteins, antisense mols. and ribozymes, in the liver. The methods find use in treating hepatic diseases or conditions. The methods also find use in treating any disease or condition in which systemic administration of the therapeutic substance, for example, a secretory protein, is desired. The methods involve administering to a mammalian patient having a need for liver expression of a therapeutic mol. an AAV vector contg. a therapeutically effective amt. of the therapeutic mol. Also provided are novel vectors employable in these methods. Expts. revealed that, following i.v. injection of AAV vectors into mice, the AAV genomes were found predominantly in the liver. The heterologous genes carried by these vectors (chimeric

cytomegalovirus promoter-lacZ or .beta.-globin promoter-globin genes) were expressed in the liver. Cotransfection of adenovirus 2-infected 293 cells with the **AAV** vectors and helper plasmid contg. cap and rep genes resulted in prodn. of 0.1-10% wild-type **AAV**. Replacement of the last 10 nucleotides of the ITR D sequence with unrelated nucleotides reduced this illegitimate recombination was reduced. Four recombinant **AAV** vectors (pD-5, pD-10, pD-15 and pD-20) with such modified ITR regions were prepd.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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PI WO 9809524 A1 19980312

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US 2003166284	A1	20030904	US 2002-109799	20020328
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AB . . . desired. The methods involve administering to a mammalian patient having a need for liver expression of a therapeutic mol. an **AAV** vector contg. a therapeutically effective amt. of the therapeutic mol. Also provided are novel vectors employable in these methods. Expts. revealed that, following i.v. injection of **AAV** vectors into mice, the **AAV** genomes were found predominantly in the liver. The heterologous genes carried by these vectors (chimeric cytomegalovirus promoter-lacZ or .beta.-globin promoter-globin genes) were expressed in the liver. Cotransfection of adenovirus 2-infected 293 cells with the **AAV** vectors and helper plasmid contg. cap and rep genes resulted in prodn. of 0.1-10% wild-type **AAV**. Replacement of the last 10 nucleotides of the ITR D sequence with unrelated nucleotides reduced this illegitimate recombination was reduced. Four recombinant **AAV** vectors (pD-5, pD-10, pD-15 and pD-20) with such modified ITR regions were prepd.

ST adeno assocd virus vector liver tropism; therapeutic gene expression liver **AAV** vector

IT Proteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study) (VP1, fusion protein with hepatitis B surface antigen, **AAV** helper virus encoding; methods and compns. for liver-specific delivery of therapeutic mols. using recombinant adeno-assocd. virus vectors)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study) (hepatitis B surface, fusion protein with **AAV** VP-1 protein, **AAV** helper virus encoding; methods and compns. for liver-specific delivery of therapeutic mols. using recombinant

adeno-assocd. virus vectors)

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

18.37

18.79

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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-1.30

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Sep 5, 2003 (20030905/UP).

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(FILE 'HOME' ENTERED AT 15:41:12 ON 11 SEP 2003)

FILE 'MEDLINE, CAPLUS' ENTERED AT 15:42:07 ON 11 SEP 2003

L1 219 S AAV AND (TARGETING OR TROPISM)

L2 143 DUP REM L1 (76 DUPLICATES REMOVED)

L3 40 S L2 AND PY<=1998

L4 1 S L3 AND (VP1 OR VP2 OR VP3)